ment and management of patients with neurodevelopmental disabilities.

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Amino Acids and Growth Hormone Manipulation

In this issue of *Nutrition*, Chromiak and Antonio[1] present an elegant and informative review of the literature regarding the use of amino acids to promote growth hormone (GH) secretion. Although strength-training athletes have used amino acids with the intention of increasing plasma GH concentration (thereby promoting skeletal muscle anabolism), it is apparent that the majority of published data does not support this proposition. Regarding the oral consumption of amino acids, approximately one-third of the published investigations has shown a significant effect of acute amino acid consumption on plasma GH. The discrepancy in results from various investigations is likely due to differences in age, sex, training status, amino acids consumed, dosages, and the mode of consumption (oral versus intravenous). Further, there is no evidence that a transient increase in plasma GH would subsequently produce gains in skeletal muscle mass with or without heavy resistance training.

Nonetheless, one could speculate that certain amino acids might confer an anabolic effect, not via an effect on plasma GH but perhaps via a direct effect on skeletal muscle protein metabolism. For instance, work by Tipton et al.[2] showed that consuming 40 g of a mixed amino acid or essential amino acid solution increases net muscle protein balance when compared with placebo. This finding suggests that consuming non-essential amino acids (found in the mixed amino acid solution) is not needed to induce an anabolic response in skeletal muscle. Rasmussen et al.[3] showed that consuming 6 g of essential amino acids with 35 g of sucrose 1 and 3 h after resistance exercise stimulates muscle protein synthesis. However, consuming this identical combination of essential amino acids and sucrose immediately before exercise produced a greater anabolic response than when taken after exercise.[4] Thus, consuming essential amino acids and sucrose before exercise induces an anabolic effect greater than that after exercise consumption.

Does the chronic consumption of amino acids (i.e., essential amino acids, mixed amino acids, or whole protein) in conjunction with exercise training confer a net gain in lean body or skeletal muscle mass? Williams et al.[5] had seven untrained subjects (median age 23 y; median weight 68.9 kg) train on a leg-extension machine five days per week for 10 wk with four sets of 10 repetitions. Alternate legs were trained on successive days. Subjects consumed a placebo or a supplement (0.8 g of glucose and 0.2 g of amino acids per kilogram of body weight) on alternate training days immediately after training. They found no significant effect of supplementation on leg extensor strength. Antonio et al.[6] investigated the effects of 6 wk of essential amino acid supplementation (average daily dose, 18.3 g/d) on exercise performance and body composition in untrained women. They found no differences between the amino acid and placebo groups with regard to body composition or muscular strength; however, the amino acid group did experience a greater increase in muscle endurance (treadmill run time to exhaustion). Interestingly, subjects consumed half of their daily dose for amino acids (or placebo) 20 min before training and within 20 min after exercise. On non-workout days (4 d/wk), they consumed the supplement or placebo in the morning. Thus, from these two investigations, it is not apparent that chronic supplementation with amino acids or a combination of amino acids and carbohydrate confers an anabolic effect. This despite the acute metabolic data demonstrated by Tipton et al.[2] and Rasmussen et al.[3] Clearly, the precise combination of amino acids

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used by those groups was not the same as the one used by Williams et al.[5] and Antonio et al.[6] Further, the use of untrained subjects[5,6] may present an important confounding variable. The training status (or lack thereof) may have masked any potential gains in lean body mass or strength. Changes in strength may be due in large part to neural adaptation rather than to skeletal muscle hypertrophy.[7]

Another interesting concept in the protein and amino acid metabolism field is "slow" versus "fast" proteins.[8] Beaufrere et al. found that, in addition to the amount of protein consumed and the amino acid composition, the speed at which a protein is digested significantly affects the ensuing net protein balance. That is, slowly digesting proteins such as casein increase total protein synthesis more than swiftly digesting proteins such as whey or an equivalent amount in free-form amino acids.

Future studies should examine how the absorption of different dietary proteins and single amino acids and amino acid combinations affect total and skeletal muscle protein synthesis. Also, future studies should examine the effect of exercise training coupled with exogenous protein and/or amino acid supplementation on the "real-world" indicators of efficacy (i.e., body composition and increased lean body mass).

For now, it is apparent that the use of amino acids to improve body composition via an effect on GH is largely ineffectual. However, there are other mechanisms in which proteins and/or amino acids might positively influence body composition.

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Hypocholesterolemic Effect of Soy Protein

The importance of dietary protein in the regulation of cholesterol metabolism has been well established in various species including humans and rats (reviewed by Huang et al.[1]). Soybean protein compared with casein with or without dietary cholesterol lowers plasma cholesterol and triacylglycerol concentrations in rats.[2,3] In humans the cholesterol-lowering effect of soybean protein is achieved only when cholesterol is included in the diet.[4]

In this issue of *Nutrition*, Kern et al.[5] compared two diets consisting of 20% by weight of protein with soy protein (92% protein) or casein (95% protein) with 1% cholesterol for 28 d in Sprague-Dawley rats. L-methionine was adjusted to be equivalent between the diets. Soy protein isolate versus casein did not significantly modify food intake, weight gain, food efficiency ratio, epididymal fat pad weight, serum triacylglycerol or high-density lipoprotein (HDL) cholesterol concentrations. However, total cholesterol was lower with the soy protein diet (−25%) than with the casein diet. Their results indicated that methionine supplementation may eliminate the decreased fat deposition previously ascribed[6] to soy protein but that methionine does not abolish the hypocholesterolemic effect of soy protein.

The hypocholesterolemic effect of soy is largely attributable to the differences in the amino acid profile of soybean protein and casein. Indeed, a major difference in the amino acid profile of soy protein versus that of casein is the methionine content, which barely represents half the amount in casein; in addition, methionine has been demonstrated to elevate serum cholesterol concentration.[7,8]

However, because methionine supplementation in the study by Kern et al. did not abolish the commonly observed hypocholesterolemic effects of soy protein relative to casein, some factor other than methionine must be at least partly responsible for the cholesterol-lowering effect of soy.

Moreover, differences between casein and soy other than their methionine content have been reported. Glycine is present at almost twice the concentration in soy protein isolate. The higher methionine:glycine ratio in casein may be responsible for elevation of serum cholesterol.[8] Glycine added to a casein diet tested on rats has been demonstrated to lower serum cholesterol concentration.[7] Although the methionine levels were equal in the diets in the study by Kern et al., the glycine difference between the sources of protein may have been responsible for the differences in serum cholesterol concentrations.

Several investigators[8,9] have suggested that the lysine:arginine ratio also may be a candidate for causing greater serum cholesterol level that occurs with casein feeding, potentially due to increased insulin sensitivity. This ratio is two-fold higher in casein than in soy protein. Lavigne et al.[10] demonstrated that soy protein as opposed to casein improves glucose tolerance and insulin sensitivity in rats. In addition, postprandial insulinemia decreased in humans who consumed soy protein versus casein.[11]

However, studies in which animals were fed amino acid mixtures simulating soybean protein or casein have suggested that some non-protein components in partly purified soybean protein may be responsible for the hypocholesterolemic effect.[12–14] Indeed, a mixture of amino acids corresponding to soybean protein exhibited higher plasma cholesterol concentrations than did the protein itself.[12] In contrast, Morita et al.[8] suggested that the pattern of amino acid composition in soy versus that in casein is responsible for the differences in cholesterol metabolism. Thus, no consensus regarding this issue has been reached.

However, when the patterns were fed as individual amino acids rather than as whole proteins, the results differed from what occurs with whole protein feeding, particularly at the digestion and intestinal absorption levels. Indeed, no significant differences in cholesterol absorption and excretion were observed between rats fed amino acid mixtures equivalent to either protein.[13]

Several studies have suggested that the hypocholesterolemic effect of vegetable proteins, in particular soybean protein, is largely attributable to higher fecal steroid excretion as a consequence of the reduction in intestinal absorption.[13,15] Iwami et al.[16] reported that soybean isolate is inferior to casein in digestibility

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